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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/564,060 | 01/10/2006 | Naoto Hagiwara | 284206US0PCT | 3962 |
| 22850 | 7590 | 10/24/2007 | EXAMINER | |
| OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314 | | | STAPLES, MARK | |
| | | ART UNIT | PAPER NUMBER | |
| | | 1637 | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/564,060 | HAGIWARA, NAOTO | |
| | Examiner | Art Unit | |
| | Mark Staples | 1637 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 30 July 2007.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-5, 7-14 and 19-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-5, 7-14, and 19-56 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____. | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

1. Applicants' amendment of claims 1, 2, 5, 9, and 12-14; the cancellation of claims 6 and 15-18; and submission of new claims 21-56 in the paper filed on 07/30/2007 is acknowledged.

Claims 1-5, 7-14, and 19-56 are pending and at issue.

Applicants' arguments filed on 07/30/2007 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

2. The submission of a non-certified English translation of JP 2003-273430 is acknowledged.

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a certified English translation of the foreign application must be submitted in reply to this action. 37 CFR 41.154(b) and 41.202(e).

Failure to provide a certified translation may result in no benefit being accorded for the non-English application.

Objections and Rejections that are Withdrawn

Drawings

3. The drawing of Figure 9 was received on 07/30/2007. This drawing is acceptable.

Claim Rejections Withdrawn - 35 USC § 112 Second Paragraph

4. The rejections of claims 5 and 12-14 under 35 USC § 112 Second Paragraph are withdrawn in light of the Applicant's amendment of these claims to clarify the relationship of the denaturation region and regeneration region within the flow channel.

Claim Rejections Moot - 35 USC § 102(b)

5. Applicant's arguments with respect to claims 1, 2, 4, 5, 7, 9, 11, 12, 14, and 19 have been considered but are moot in view of the new ground(s) of rejection. The rejections of claims 1, 2, 4, 5, 7, 9, 11, 12, 14, and 19 under 35 USC § 102(b) are moot. New rejections are given below.

Claim Rejections Moot - 35 USC § 103(a)

6. Applicant's arguments with respect to claims 3, 8, 10, 13, 19, and 20 have been considered but are moot in view of the new ground(s) of rejection. The rejections of claims 3, 6, 8, 10, 13, 19, and 20 under 35 USC § 103(a) are moot. New rejections are given below.

Cancelled Claims

7. The rejections of claims 6 and 15-18 are moot, as these claims are cancelled.

New Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 103

8. Claims 1, 2, 4, 5, 7, 9, 11-14, 19, 21, 24, 25, 27-31, 33-38, 40-50, and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Misako et al. (JP 2003-174900, published on 24.06.2003, previously cited) and Schelper et al. (1997, previously cited).

Regarding claims 1, 2, 7, 27-31, 34, 36, 37, 40-43, 48-50, and 56, Misako et al. teach a nucleic acid amplification device comprising a first treatment chamber wherein a sample solution containing nucleic acid is heated and the nucleic acid therein is denatured into single strands, a second treatment chamber wherein the single-stranded nucleic acid obtained in the aforementioned first treatment chamber is annealed to a primer, and a third treatment chamber wherein DNA polymerase acts upon the nucleic acid obtained in the second treatment chamber and a lengthening reaction is performed thereby. In addition, Misako et al. describe the immobilization of the DNA polymerase, a nucleic acid synthetase, in the reaction vessel and the formation of a circulatory flow route containing the aforementioned first, second, and third treatment chambers in the device (see especially Claims 11 to 13; Figure 3).

Regarding claims 4, 24, 25, and 33, Misako et al. teach that polymerase is immobilized on an inner wall surface, since the DNA polymerase is fixed in the reactor

where the amplification takes place. The amplification components being fluid must be contained within the reactor (see especially Claims 11 to 13; paragraph 0023; and Figure 3).

Regarding claims 5, 12, 13, and 14, The "first treatment chamber" of Misako et al. is equivalent to the "denaturation region" of this application, and the "second treatment chamber" and "third treatment chamber" are formed in succession and are equivalent to the "regeneration region" of the instant application.

Regarding claims 21 and 50, Misako et al. teach that the number of cycles can be in the range of one to 40 (see paragraph 0068) which encompasses the range of 20 to 40 cycles of the instant claim.

Regarding claim 19; Misako et al. teach that the flow channel can comprise either the denaturation region or the regeneration region.

Furthermore, the PCR method wherein a heating cycle is performed between two temperatures by performing annealing and a lengthening reaction simultaneously at the same temperature was widely known technology at the time this application was filed (as evidenced by Biotechniques, 1993, 14(3), p. 390-4, cited on the Information Disclosure Statement, IDS).

Misako et al. teach as noted above.

Regarding claims 1 and 9, Misako et al. teach a nucleic acid synthetase but do not specifically teach one which has a temperature optimum between 30 to 40°C.

Further regarding claim 30, Misako et al. teach that reagent volumes can be varied and also as referenced (see paragraph 0006) to U.S. Patent Nos. 4,683,195, 4,683,202 and 4,965,188. The device of Misako et al. is capable of performing the intended use of varying volume, thus it meets the claim limitation. Further regarding claims 27 and 56, Misako et al. teach a device of various dimensions capable of performing the intended use of the device of the instant claims. The specific dimensions recited in instant claim 56 are not critical to the claimed invention. The specific dimension are obvious as a one of many design choices.

Regarding claims 1, 9, and 35 and further regarding claims 28, 29, and 44-47, Schelper et al. teach: "The temperature optimum of C. symbiosum polymerase [a type of nucleic acid synthetase] in our activity assay was found to be between 38°C and 42°C" (see 4th sentence of 1st full paragraph on p. 7810) which overlaps the 30 to 40°C range of the instant claims.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the device of Misako et al. by using a polymerase with a temperature optimum in the range of 38 to 40°C and using that temperature optimum as suggested by Schelper et al. with a reasonable expectation of success. The motivation to do so is provided by Schelper et al. who teach nucleic acid amplification can be accomplished by a polymerase with a temperature optimum in the range of 38 to 40°C. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Although these are new rejections necessitated by amendment, it is noted that Applicant has argued that the synthetase of Schelper et al. would not be obvious to try in the methods of Misako et al. Applicant's argument is not persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., reliable or optimal amplification) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Furthermore, Schelper et al. teach a *C. symbiosum* polymerase which is a synthetase that amplifies DNA natively and in assay (see Figure 4). It is obvious that a polymerase can be used in a polymerase chain reaction (PCR) as taught by Misako et al. Yet, Applicant argues that there is no specific teaching/motivation in either reference to use the polymerase of Schelper et al. as the polymerase in methods of Misako et al. However, KSR forecloses Appellant's argument that a specific teaching is required for a finding of obviousness. KSR, 127 S.Ct. at 1741, 82 USPQ2d at 1396 (as given in the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. App. & Interf. June 25, 2007 and available at <http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>).

9. Claims 3, 10, 13, 20, 22, 23, 32, 39, 51-54, are rejected under 35 U.S.C. 103(a) as being unpatentable over Misako et al. and Schelper et al. as applied to claims 1, 2, 21, and 30 above, and further in view of Moses et al. (1994 previously cited).

Misako et al. and Schelper et al. teach as noted above.

Regarding claims 3 and 10, Misako et al. teach immobilizing a polymerase but do not specifically teach immobilizing a polymerase or other nucleic acid synthetase on beads.

Regarding claim 13 and as noted above, Misako et al. teach that the flow channel can comprise either the denaturation region or the regeneration region.

Regarding claim 20 and as noted above, Misako et al. teach that the flow channel can comprise the denaturation region and the regeneration region.

Regarding claim 25 and as noted above, Misako et al. teach that the synthetase is immobilized on the inner wall of the regeneration region.

Regarding claims 3, 10, 22, 32, and 51, Moses et al. teach DNA polymerase, a type of synthetase, bound to beads which fill a column (entire reference, especially Figure 2).

Regarding claims 23, 52-54, Moses et al. teach two types/forms of DNA polymerase, a type of synthetase (see Abstract).

Further regarding claim 53 and 54, as Misako et al. teach synthetases can be immobilized on a surface/inner wall and Moses et al. teach that two types of synthetases can be immobilized on beads which is a type of surface, it was obvious

from the teaching of Misako et al. in view of Moses et al. that two synthetases could be immobilized on a surface/inner wall.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the device of Misako et al. and Schelper et al. by immobilizing a nucleic acid synthetase on beads as suggested by Moses et al. with a reasonable expectation of success. The motivation to do so is provided by Moses et al. who teach that the polymerase can be bound to beads, retain activity and that reagents can be passed over the beads. Further motivation is provided by Misako et al. who teach that immobilized polymerase can be used to amplify DNA. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

10. Claims 5 and 12-14 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Misako et al. and Schelper et al. as applied to claims 1, 2, and 4 above, and further in view of Hideo et al. (JP 6-30776 A, published on 08.02.1994, previously cited).

Misako et al. and Schelper et al. teach as noted above.

Misako et al. teach denaturation and regeneration regions but do not teach where they alternate each other in the flow channel.

Regarding claims 5 and 12-14, Hideo et al. teach where denaturation and regeneration regions alternate each other in the flow channel (especially Figures 1 and 2 and where in Figure 2 the coil involves more than one loop and thus inherently

alternates the denaturation and regeneration regions. It is further noted that Figure 2 of Hideo et al. is the same construction as Figure 5 of the instant application and they achieve the same thing, alternating regions of denaturation and regeneration).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the device of Misako et al. and Schelper et al. alternating regions of denaturation and regeneration as suggested by Hideo et al. with a reasonable expectation of success. The motivation to do so is provided by Hideo et al. who teach that coils can be used to have flow going through alternating regions of denaturation and regeneration. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

11. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Misako et al. and Schelper et al. as applied to claim 1 above, and further in view of Southgate et al. (US Patent No: 5,863,801, issued 1999, previously cited).

Misako et al. and Schelper et al. teach as noted above.

Misako et al. teach a flow device but do not specifically teach a flow device in which the flow direction can be reversed.

Southgate et al. teach a device with reverse flow (see paragraph 114 which describes Figure 6).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the device of Misako et al. and Schelper et al. by incorporating reverse flow as suggested by Southgate et al. with a reasonable

expectation of success. The motivation to do so is provided by Southgate et al. who teach reversing flow in a device can be used to suspend beads in that device to allow better mixing of the sample with beads. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

12. Claims 26 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Misako et al. and Schelper et al. as applied to claims 1 and 30 above, and further in view of Belfort (1988).

Misako et al. and Schelper et al. teach as noted above.

Misako et al. and Schelper et al. do not teach a flow channel comprising a semi-permeable capillary.

Regarding claims 26 and 55, Belfort teaches flow channels with semi-permeable/permselective membranes capillaries (entire article, especially Figure 5, its description in the 1st paragraph on p. 1051 and the teaching at the bottom of p. 1052 continued to p. 1053: "In the standard design, many hollow fiber membranes are potted together at each end and sealed in a housing (usually tubular in design) so as to separate the extracapillary space (ECS) from the lumen space . . .").

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the flow channel of Misako et al. and Schelper et al. by using semi-permeable/permselective membranes capillaries as suggested by Belfort with a reasonable expectation of success. The motivation to do so is provided by Belfort who teaches: ". . . reactions are conducted in solution by the

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whole cells or enzymes and the membranes act solely as selective barriers" (see 1st sentence on p. 1061). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

13. No claim is free of the prior art.
14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-

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9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples
Examiner
Art Unit 1637
October 16, 2007

KRH
KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

10/17/07